

Inventor(s): BOUCHARD *et al.*
Application No.: 08/786,937
Attorney Docket No.: 098501-0235299

II. AMENDMENTS TO THE CLAIMS

1-37. (Canceled)

38. (Currently Amended) A method for obtaining the production of a fertilizable oocyte within a program of controlled ovarian stimulation for assisted reproduction techniques (COS/ART) comprising:

- (a) administering an exogenous gonadotropin to induce follicle growth, and
- (b) administering a luteinizing hormone releasing hormone (LHRH) antagonist to prevent a premature LH surge, wherein the LHRH antagonist is administered in a single or dual dosage regimen of from 1 to 10 mg per dose beginning on menstruation cycle day 1 to 10; and

whereby wherein follicular growth occurs in the absence of a LH surge and [,] a fertilizable oocyte is produced, ovulation occurs between day 9 and 20 of the menstruation cycle, and the LHRH antagonist is sufficient to suppress LH, while FSH secretion is maintained at a natural level and individual estrogen development is not affected.

39. (Previously Presented) The method of claim 38, wherein the dosage of LHRH antagonist is in the range of 2-6 mg per dose.

40. (Previously Presented) The method of claim 38, wherein dosage of LHRH antagonist is 3 mg per dose.

41. (Cancel)

42. (Previously Presented) The method of claim 38, wherein the LHRH antagonist is administered by subcutaneous injection.

43. (Cancel)

44. (Currently Amended) The method of ~~claim 43~~ claim 38, wherein the LHRH antagonist is administered starting cycle day 4 to 8.

45. (Currently Amended) The method of ~~claim 43~~ claim 38, wherein the LHRH antagonist is administered starting on cycle day 6 to 10 and ovulation occurs between day 9-16 of the menstruation cycle.

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46. (Currently Amended) The method of ~~claim 43~~ claim 38, wherein ovulation occurs within 6.5 days following administration of a single or second dose of the LHRH antagonist.

47. (Currently Amended) The method of ~~claim 43~~ claim 38, wherein ovulation occurs normally, without the administration of a hormone or hormone agonist to induce ovulation.

48. (Currently Amended) The method of ~~claim 43~~ claim 38, wherein ovulation is induced by administering a hormone or hormone agonist in order to induce ovulation.

49. (Currently Amended) The method of ~~claim 43~~ claim 38, wherein ovulation is induced by administering a hormone or hormone agonist selected from the group consisting of native LH, recombinant LH, an LHRH agonist, and HCG.

50. (Previously Presented) The method of claim 38, wherein the LHRH antagonist is: Cetrorelix.

51. (Currently Amended) A method for obtaining the production of a fertilizable oocyte within a program of COS/ART comprising:

(a) administering human menopausal gonadotropin (HMG) to induce follicle growth, and

(b) administering Cetrorelix to prevent a premature LH surge, wherein Cetrorelix is administered in a single or dual dosage regimen of ~~from~~ 1 to 10 mg per dose beginning on menstruation cycle day 1 to 10; and

whereby follicular growth occurs in the absence of a LH surge and [[,]] a fertilizable oocyte is produced, ovulation occurs between day 9 and 20 of the menstruation cycle, and the Cetrorelix is sufficient to suppress LH, while FSH secretion is maintained at a natural level and individual estrogen development is not affected.

52. (Currently Amended) The method of ~~claim 49~~ claim 51, wherein the dosage of the LHRH antagonist is in the range of 2-6 mg per dose.

53. (Currently Amended) The method of claim 51, wherein the dosage of ~~LHRH~~ antagonist Cetrorelix is 3 mg per dose.

54. (Cancel)

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55. (Cancel)

56. (Currently Amended) The method of ~~claim 55~~ claim 51, wherein the ~~LHRH~~ antagonist Cetrorelix is administered starting cycle day 4 to 8.

57. (Currently Amended) The method of ~~claim 55~~ claim 51, wherein Cetrorelix is administered starting on cycle day 6 to 10 and ovulation occurs between day 9-16 of the menstruation cycle.

58. (Currently Amended) The method of ~~claim 55~~ claim 51, wherein ovulation occurs within 6.5 days following administration of a single or second dose of Cetrorelix.

59. (Currently Amended) The method of ~~claim 55~~ claim 51, wherein ovulation occurs normally, without the administration of a hormone or hormone agonist to induce ovulation.

60. (Currently Amended) The method of ~~claim 55~~ claim 51, wherein ovulation is induced by administering a hormone or hormone agonist selected from the group consisting of native LH, recombinant LH, an LHRH agonist, and HCG.

61. (Currently Amended) An improved method for obtaining the production of a fertilizable oocyte within a program of COS/ART comprising:

(a) administering an exogenous gonadotropin to induce follicle growth; and

(b) administering an LHRH antagonist to prevent a premature LH surge;

whereby follicular growth occurs in the absence of a LH surge and a fertilizable oocyte is produced;

wherein the improvement comprises administering the LHRH antagonist in a single or dual dosage regimen of ~~from~~ 1 to 10 mg per dose beginning on menstruation cycle day 1 to 10, and wherein the follicular growth occurs in the absence of a LH surge, a fertilizable oocyte is produced, ovulation occurs between day 9 and 20 of the menstruation cycle, and the LHRH antagonist is sufficient to suppress LH, while FSH secretion is maintained at a natural level and individual estrogen development is not affected.

62. (Previously Presented) The improved method of claim 61, wherein the dosage of LHRH antagonist is in the range of 2-6 mg per dose.

63. (Previously Presented) The improved method of claim 61, wherein the dosage of LHRH antagonist is 3 mg per dose.

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64. (Cancel)
65. (Previously Presented) The improved method of claim 61, wherein the LHRH antagonist is administered by subcutaneous injection.
66. (Cancel)
67. (Currently Amended) The improved method of ~~claim 66~~ claim 61, wherein the LHRH antagonist is administered starting cycle day 4 to 8.
68. (Currently Amended) The improved method of ~~claim 66~~ claim 61, wherein the LHRH antagonist is administered starting on cycle day 6 to 10 and ovulation occurs between day 9-16 of the menstruation cycle.
69. (Currently Amended) The improved method of ~~claim 66~~ claim 61, wherein ovulation occurs within 6.5 days following administration of a single or second dose of the LHRH antagonist.
70. (Currently Amended) The improved method of ~~claim 66~~ claim 61, wherein ovulation occurs normally, without the administration of a hormone or hormone agonist to induce ovulation.
71. (Currently Amended) The improved method of ~~claim 66~~ claim 61, wherein ovulation is induced by administering a hormone or hormone agonist selected from the group consisting of native LH, recombinant LH, an LHRH agonist, and HCG.
72. (Previously Presented) The improved method of claim 61, wherein the LHRH antagonist is Cetrorelix.
73. (Currently Amended) The improved method of claim 61 further comprising:
(a) administering human menopausal gonadotropin (HMG) to induce follicle growth; and
(b) administering Cetrorelix to prevent a premature LH surge;
wherein the improvement comprises subcutaneously administering Cetrorelix in a single or dual dosage regimen of ~~from~~ 1 to 10 mg per dose beginning on menstruation cycle day 1 to 10; and
whereby ovulation occurs between day 9 and 20 of the menstruation cycle, and the

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LHRH antagonist is sufficient to suppress LH, while FSH secretion is maintained at a natural level and individual estrogen development is not affected.

74. (Previously Presented) The improved method of claim 73, wherein the dosage of Cetorelix is in the range of 2-6 mg per dose.

75. (Previously Presented) The improved method of claim 73, wherein the dosage of LHRH antagonist is 3 mg per dose.

76. (Cancel)

77. (Cancel)

78. (Currently Amended) The improved method of ~~claim 77~~ claim 73, wherein the LHRH antagonist is administered starting cycle day 4 to 8.

79. (Currently Amended) The improved method of ~~claim 77~~ claim 73, wherein Cetorelix is administered starting on cycle day 6 to 10 and ovulation occurs between day 9-16 of the menstruation cycle.

80. (Currently Amended) The improved method of ~~claim 77~~ claim 73, wherein ovulation occurs within 6.5 days following administration of a single or second dose of Cetorelix.

81. (Currently Amended) The improved method of ~~claim 77~~ claim 73, wherein ovulation occurs normally, without the administration of a hormone or hormone agonist to induce ovulation.

82. (Currently Amended) The improved method of ~~claim 77~~ claim 73, wherein ovulation is induced by administering a hormone or hormone agonist selected from the group consisting of native LH, recombinant LH, an LHRH agonist, and HCG.

83. (Currently Amended) A method for obtaining the production of a fertilizable oocyte within a program of controlled ovarian stimulation for assisted reproduction techniques (COS/ART) comprising

(a) administering an exogenous gonadotropin to induce follicle growth,

(b) administering a luteinizing hormone releasing hormone (LHRH) antagonist to prevent a premature LH surge, wherein the LHRH antagonist is administered in a dosage regimen of daily doses of 0.25 mg/day for multiple days;

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~~whereby follicular growth occurs in the absence of a LH surge and a fertilizable oocyte is produced;~~

wherein the LHRH antagonist is administered daily beginning on menstruation cycle day 1 to 10, wherein the follicular growth occurs in the absence of a LH surge, a fertilizable oocyte is produced, ovulation occurs between day 9 and 20 of the menstruation cycle, and the LHRH antagonist is sufficient to suppress LH, while FSH secretion is maintained at a natural level and individual estrogen development is not affected.

84. (Previously Presented) The method of claim 83, wherein the LHRH antagonist is administered by subcutaneous injection.

85. (Canceled)

86. (Currently Amended) The method of ~~claim 85~~ claim 83, wherein the LHRH antagonist is administered starting cycle day 4 to 8.

87. (Currently Amended) The method of claim 83, wherein a daily dose of the LHRH antagonist is administered for ~~from~~ 3 to 14 days.

88. (Currently Amended) The method of claim 83, wherein a daily dose of the LHRH antagonist is administered for ~~from~~ 3 to 7 days.

89. (Currently Amended) The method of ~~claim 85~~ claim 83, wherein ovulation occurs normally, without the administration of a hormone or hormone agonist to induce ovulation.

90. (Currently Amended) The method of ~~claim 85~~ claim 83, wherein ovulation is induced by administering a hormone or hormone agonist selected from the group consisting of native LH, recombinant LH, an LHRH agonist, and HCG.

91. (Previously Presented) The method of claim 83, wherein the LHRH antagonist is Cetrorelix.

92. (Currently Amended) A method for obtaining the production of a fertilizable oocyte within a program of COS/ART comprising:

(a) administering human menopausal gonadotropin (HMG) to induce follicle growth, and;

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(b) administering Cetorelix to prevent a premature LH surge, wherein Cetorelix is subcutaneously administered in a dosage regimen of daily doses of 0.25 mg per day for multiple days;

whereby follicular growth occurs in the absence of a LH surge and ~~[[,]]~~ a fertilizable oocyte is produced, ovulation occurs between day 9 and 20 of the menstruation cycle, and the Cetorelix is sufficient to suppress LH, while FSH secretion is maintained at a natural level and individual estrogen development is not affected.

93. (Canceled)

94. (Currently Amended) The method of ~~claim 93~~ claim 92, wherein Cetorelix is administered starting cycle day 4 to 8.

95. (Currently Amended) The method of ~~claim 93~~ claim 92, wherein a daily dose of Cetorelix is administered for ~~from~~ 3 to 14 days.

96. (Currently Amended) The method of ~~claim 93~~ claim 92, wherein a daily dose of Cetorelix is administered for ~~from~~ 3 to 7 days.

97. (Currently Amended) The method of ~~claim 93~~ claim 92, wherein ovulation occurs normally, without the administration of a hormone or hormone agonist to induce ovulation.

98. (Currently Amended) The method of ~~claim 93~~ claim 92, wherein ovulation is induced by administering a hormone or hormone agonist selected from the group consisting of native LH, recombinant LH, an LHRH agonist, and HCG.

99. (Currently Amended) An improved method for obtaining the production of a fertilizable oocyte within a program of controlled ovarian stimulation for assisted reproduction techniques (COS/ART) comprising

(a) administering an exogenous gonadotropin to induce follicle growth, and

(b) administering a luteinizing hormone releasing hormone (LHRH) antagonist to prevent a premature LH surge,

~~whereby follicular growth occurs in the absence of a LH surge and a fertilizable oocyte is produced;~~

wherein the improvement comprises administering the LHRH antagonist in a dosage regimen of daily doses of 0.25 mg per day for multiple days, the follicular growth occurs in

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the absence of a LH surge, a fertilizable oocyte is produced, ovulation occurs between day 9 and 20 of the menstruation cycle, and the LHRH antagonist is sufficient to suppress LH, while FSH secretion is maintained at a natural level and individual estrogen development is not affected.

100. (Previously Presented) The improved method of claim 99, wherein the LHRH antagonist is administered by subcutaneous injection.

101. (Canceled)

102. (Currently Amended) The improved method of ~~claim 101~~ claim 99, wherein the LHRH antagonist is administered starting cycle day 4 to 8.

103. (Currently Amended) The improved method of ~~claim 101~~ claim 99, wherein a daily dose of the LHRH antagonist is administered for ~~from~~ 3 to 14 days.

104. (Currently Amended) The improved method of ~~claim 101~~ claim 99, wherein a daily dose of the LHRH antagonist is administered for ~~from~~ 3 to 7 days.

105. (Currently Amended) The improved method of ~~claim 101~~ claim 99, wherein ovulation occurs normally, without the administration of a hormone or hormone agonist to induce ovulation.

106. (Currently Amended) The improved method of ~~claim 101~~ claim 99, wherein ovulation is induced by administering a hormone or hormone agonist selected from the group consisting of native LH, recombinant LH, an LHRH agonist, and HCG.

107. (Previously Presented) The improved method of claim 99, wherein the LHRH antagonist is: Cetorelix.

108. (Currently Amended) The improved method of claim 99, comprising:

(a) administering human menopausal gonadotropin (HMG) to induce follicle growth,
and

(b) administering Cetorelix to prevent a premature LH surge;

wherein the improvement comprises subcutaneously administering Cetorelix in a dosage regimen of daily doses of 0.25 mg per day for multiple days;

whereby follicular growth occurs in the absence of a LH surge and a fertilizable oocyte is produced, ovulation occurs between day 9 and 20 of the menstruation cycle, and the

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Cetrorelix is sufficient to suppress LH, while FSH secretion is maintained at a natural level and individual estrogen development is not affected.

109. (Canceled)

110. (Currently Amended) The improved method of ~~claim 109~~ claim 108, wherein Cetrorelix is administered starting cycle day 4 to 8.

111. (Currently Amended) The improved method of ~~claim 109~~ claim 108, wherein a daily dose of Cetrorelix is administered for ~~from~~ 3 to 14 days.

112. (Currently Amended) The improved method of ~~claim 109~~ claim 108, wherein a daily dose of Cetrorelix is administered for ~~from~~ 3 to 7 days.

113. (Currently Amended) The improved method of ~~claim 109~~ claim 108, wherein ovulation occurs normally, without the administration of a hormone or hormone agonist to induce ovulation.

114. (Currently Amended) The improved method of ~~claim 109~~ claim 108, wherein ovulation is induced by administering a hormone or hormone agonist selected from the group consisting of native LH, and recombinant LH, ~~an LHRH agonist, and HCG.~~

115. (Currently Amended) A method for obtaining the production of a fertilizable oocyte within a program of assisted reproduction techniques comprising:

(a) allowing normal follicular growth and development to proceed in the absence of stimulation by an exogenous gonadotropin;

(b) administering a luteinizing hormone releasing hormone (LHRH) antagonist in a single or dual dosage regimen that prevents a premature LH surge;

whereby follicular growth and development proceeds in the absence of a LH surge and a fertilizable oocyte is produced, ovulation occurs between day 9 and 20 of the menstruation cycle, and the Cetrorelix is sufficient to suppress LH, while FSH secretion is maintained at a natural level and individual estrogen development is not affected.

116. (Previously Presented) The method of claim 115, wherein the LHRH antagonist is administered by subcutaneous injection.

117. (Canceled)

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118. (Currently Amended) The method of ~~claim 117~~ claim 115, wherein the LHRH antagonist is administered starting cycle day 4 to 8.

119. (Currently Amended) The method of ~~claim 117~~ claim 115, wherein the LHRH antagonist is administered starting on cycle day 6 to 10 and ovulation occurs between day 9 to 16 of the menstruation cycle.

120. (Currently Amended) The method of ~~claim 117~~ claim 115, wherein ovulation occurs within 6.5 days following administration of a single or second dose of the LHRH antagonist.

121. (Currently Amended) The method of ~~claim 117~~ claim 115, wherein ovulation occurs normally, without the administration of a hormone or hormone agonist to induce ovulation.

122. (Currently Amended) The method of ~~claim 117~~ claim 115, wherein ovulation is induced by administering a hormone or hormone agonist in order to induce ovulation.

123. (Currently Amended) The method of ~~claim 117~~ claim 115, wherein ovulation is induced by administering a hormone or hormone agonist selected from the group consisting of native LH, recombinant LH, an LHRH agonist, and HCG.

124. (Currently Amended) The method of ~~claim 117~~ claim 115, wherein the LHRH antagonist is selected from the group consisting of Ganirelix, Antarelix, Antide, Azaline B, Famorelix, A-76154, Nal-Glu, 88-88, Cetrorelix, a structure-truncated peptide with LHRH-antagonistic activity, a peptidomimetic with LHRH-antagonistic activity, and a bicyclic LHRH-analog with antagonistic activity.

125. (Previously Presented) The method of claim 124, wherein the LHRH antagonist is a peptidomimetic with LHRH-antagonistic activity selected from the group consisting of D-23980 and D-24824.

126. (Previously Presented) The method of claim 124, wherein the LHRH antagonist is: Cetrorelix.

127. (Currently Amended) The method of ~~claim 117~~ claim 115, wherein a fertilizable oocyte is produced within a program of extracorporeal fertilization by sperm injection.

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128. (Currently Amended) The method of ~~claim 117~~ claim 115, wherein a fertilizable oocyte is produced within a program of extracorporeal fertilization by *in vitro* fertilization.